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IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF	:
NOBUKAZU TANAKA, ET AL.	: EXAMINER: MILLIGAN, ADAM C.
SERIAL NO: 10/576,257	:
FILED: APRIL 27, 2007	: GROUP ART UNIT: 1612
FOR: TABLET QUICKLY DISINTEGRATING IN ORAL CAVITY	:

DECLARATION UNDER 37 C.F.R. § 1.132

COMMISSIONER FOR PATENTS
ALEXANDRIA, VIRGINIA 22313

SIR:

Now comes Mr. Nobukazu TANAKA who states that:

1. I am a named inventor of the above-identified application.

2. I have been employed by Fuji Chemical Industry Co., Ltd., for 24 years as a scientific researcher in the field of pharmaceuticals.

3. I understand the English language, or at least the contents of the Declaration were made clear to me prior to executing the same.

4. The comparative experimental data presented in the following Table A demonstrates that superior properties with respect to an excellent balance of both improved oral disintegration times and tabletting properties are exhibited by a composition having a weight ratio of mannitol to other

saccharide(s) of (98-75) : (2-25) in accordance with the present invention, as compared to the inferior properties exhibited by a conventional composition having a weight ratio of mannitol to other saccharide(s) outside (98-75) : (2-25).

5. Experimental Results:

Table A

Tablet Composition	Comparative Example A	Example B	Example 9	Example C	Comparative Example D
Weight Ratio of mannitol : lactose	100 : 0	98 : 2	90 : 10	75 : 25	65 : 35
Mannitol	280	274.4	252	210	182
Lactose	0	5.6	28	70	98
Crystalline cellulose	60	60	60	60	60
Crospovidone	32	32	32	32	32
Mg aluminometasillicate	28	28	28	28	28
Tabletting Pressure (kgf)	340	380	310	260	240
Oral Disintegration Time (sec)	16	26	17	34	**73**
Tabletting troubles	**Yes***	No	No	No	No

* The tablet composition stuck to the punches, and the shape of the obtained tablets was not satisfactory.

6. The hardness value for each of the Tablets is 3.5 kg and the tabletting pressure was varied for each tablet to achieve a consistent hardness value for each tablet. Generally, the disintegration time is measured for tablets having the same hardness because it is well known in the field that varying tablet hardness effects the disintegration time and so as to insure that the effects observed were a result of the composition and not the hardness.

7. The tablet compositions of Examples B and C, and Comparative Examples A and D, were prepared according Example 9 in the present specification, with the exception of alternatively containing mannitol and the other saccharide(s) in the weight ratio specified in Table A above.

8. This evidence clearly demonstrates that the tablet compositions of Examples B, 9 and C, which contain mannitol and other saccharide(s) in the weight ratio of (98-75) : (2-25) in accordance with the present invention, exhibit superior properties with respect to an excellent balance of both improved oral disintegration times and tabletting properties, as compared to the inferior tabletting property exhibited by the tablet composition of Comparative Example A, which has a weight ratio of mannitol and other saccharide(s) of (100) : (0), and the inferior oral disintegration time property exhibited by the tablet composition of Comparative Example D, which has a weight ratio of mannitol and other saccharide(s) of (65) : (3), which is similar to the weight ratio described in Koike.

9. In my opinion, Examples similar in composition to Examples B, 9 and C above, but containing, in place of lactose, other saccharide(s) selected from sorbitol, erythritol, maltitol, sucrose, glucose, fructose, maltose, trehalose, paratinit and paratinose, would exhibit comparable properties to those of Examples B, 9 and C above with respect to an excellent balance of both improved oral disintegration times and tabletting properties (See e.g., the Table at page 30 of the present specification). I am aware of no reason to believe otherwise. More specifically, the tablets should have (1) superior oral disintegration time, (2) appropriate tablet hardness, (3) tabletting pressure, and (4) useful tablets at the end.

10. If the tablets do not have an appropriate hardness (typically about 3 kg or above), the tablets are friable making it difficult to manufacture, store and transport the tablet. However, if the tableting pressure is too high (e.g., 2000 kgf), too high a load is placed on the apparatus used for

manufacture causing deleterious effects on the machine. Further, when placing such a high load on the tablets, the resultant tablets are typically broken, chipped or cracked and have little commercial value.

11. I understand that the U.S. patent Examiner has stated "given the disintegration time of the claimed range falls within the comparative examples A and D" which he has explained to mean that the two comparative examples demonstrate weight ratios of mannitol to lactose above and below the claimed range, each resulting in a oral disintegration time above and below the inventive examples B, 9 and C. Accordingly, the Examiner concludes that optimizing the ratio between comparative Examples A and D would have yielded an expectation for the oral disintegration times demonstrated for inventive examples B, 9 and C. However, the present application demonstrates that the ratio of mannitol and lactose as claimed in claim 1 yields an improved tablet having an excellent balance (1) superior oral disintegration time, (2) appropriate tablet hardness, (3) tabletting pressure, and (4) useful tablets at the end.

12. In short, Comparative Example D did not result in a tablet with sufficient oral disintegration time and Comparative Example A, while having satisfactory disintegration, produced tablets have the negative effects of sticking and binding, meaning that the tablets are unsuitable for commercial use. Therefore, while each of Comparative Examples A and D had different problems, the ratio of mannitol and lactose defined in Claim 1 solved these problems giving the excellent balance of properties required for a suitable final tablet.

13. The undersigned declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are

punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

Nobukazu Tanaka
Signature of Mr. Nobukazu TANAKA

Feb. 1, 2011
Date